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# MEDICAL POLICY – 5.01.620 Vascular Endothelial Growth Factor (VEGF) Receptor Inhibitors for Ocular Disorders

BCBSA Ref. Policy:	9.03.31	
Effective Date:	Apr. 1, 2025	RELATED MEDICAL POLICIES:
Last Revised:	March 11, 2025	None
Replaces:	N/A	

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### Introduction

Age-related macular degeneration is due to a small area of the retina called the macula being impaired as people age. This results in loss of vision overtime. There are two types of age-related macular degeneration called the dry form and the wet form. The dry form is caused by deposits in the macula and the wet form is caused by the creation of new blood vessels underneath the macula. There are drugs called vascular endothelial growth factor (VEGF) receptor inhibitors that interfere with the growth of blood vessels in the wet form of age-related macular degeneration. These drugs can also help other conditions of the eye that are related to the blood vessels. This policy describes when Beovu, Byooviz, Cimerli, Eylea, Eylea HD, Lucentis, Macugen, Susvimo, and Vabysmo may be considered medically necessary.

**Note:** The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

### **Policy Coverage Criteria**

Drug	Medical Necessity	
Beovu (brolucizumab-dbll)	<ul> <li>Beovu (brolucizumab-dbll) may be considered medically necessary for the following:</li> <li>Neovascular (Wet) Age-Related Macular Degeneration (AMD)</li> <li>Diabetic Macular Edema (DME)</li> <li>AND</li> <li>The individual has tried bevacizumab and had an inadequate response or intolerance to bevacizumab</li> <li>AND</li> <li>Per each eye treated, Beovu (brolucizumab-dbll) is not used in combination with Byooviz (ranibizumab-nuna), Cimerli (ranibizumab-eqrn), Eylea/Eylea HD (aflibercept), Lucentis (ranibizumab), Macugen (pegaptanib), Pavblu (aflibercept-ayyh), Susvimo (ranibizumab), or Vabysmo (faricimab-svoa)</li> </ul>	
	<b>Note:</b> For bevacizumab no review is needed for eye-related injections. Reference to bevacizumab includes the biosimilars (e.g., bevacizumab- adcd, bevacizumab-awwb, bevacizumab-bvzr, and bevacizumab-maly)	
Byooviz (ranibizumab-	Byooviz (ranibizumab-nuna) may be considered medically	
nuna)	<ul> <li>necessary for the following:</li> <li>Neovascular (Wet) Age-Related Macular Degeneration (AMD)</li> <li>Macular Edema Following Retinal Vein Occlusion (RVO)</li> <li>Myopic Choroidal Neovascularization (mCNV)</li> <li>AND</li> </ul>	
	<ul> <li>The individual has tried bevacizumab and had an inadequate response or intolerance to bevacizumab</li> <li>AND</li> </ul>	
	<ul> <li>Per each eye treated, Byooviz (ranibizumab-nuna) is not used in combination with Beovu (brolucizumab-dbll), Eylea/Eylea HD (aflibercept), Macugen (pegaptanib), Pavblu (aflibercept-ayyh), Susvimo (ranibizumab), or Vabysmo (faricimab-svoa)</li> </ul>	
	<b>Note:</b> For bevacizumab no review is needed for eye-related injections. Reference to bevacizumab includes the biosimilars (e.g., bevacizumab- adcd, bevacizumab-awwb, bevacizumab-bvzr, and bevacizumab-maly)	
Cimerli (ranibizumab-eqrn)	Cimerli (ranibizumab-eqrn) may be considered medically necessary for the following:	

Drug	Medical Necessity	
	<ul> <li>Neovascular (Wet) Age-Related Macular Degeneration (AMD)</li> <li>Macular Edema Following Retinal Vein Occlusion (RVO)</li> <li>Diabetic Macular Edema (DME)</li> <li>Diabetic Retinopathy (DR)</li> <li>Myopic Choroidal Neovascularization (mCNV)</li> <li>AND</li> <li>The individual has tried bevacizumab and had an inadequate response or intolerance to bevacizumab</li> <li>AND</li> <li>Per each eye treated, Cimerli (ranibizumab-eqrn) is not used in combination with Beovu (brolucizumab-dbll), Eylea/Eylea HD (aflibercept), Macugen (pegaptanib), Pavblu (aflibercept-ayyh), Susvimo (ranibizumab), or Vabysmo (faricimab-svoa)</li> </ul>	
	<ul> <li>Note: For bevacizumab no review is needed for eye-related injections.</li> <li>Reference to bevacizumab includes the biosimilars (e.g., bevacizumab-adcd, bevacizumab-awwb, bevacizumab-bvzr, and bevacizumab-maly)</li> </ul>	
Eylea (aflibercept)	Eylea (aflibercept) may be considered medically necessary for	
	the following:	
	Neovascular (Wet) Age-Related Macular Degeneration (AMD)	
	<ul> <li>Diabetic Macular Edema (DME)</li> <li>Diabetic Retinonathy (DR)</li> </ul>	
	<ul> <li>Diabetic Retinopathy (DR)</li> <li>Macular Edema Following Retinal Vein Occlusion (RVO)</li> </ul>	
	AND	
	• The individual has tried bevacizumab and had an inadequate response or intolerance to bevacizumab	
	AND	
	<ul> <li>Per each eye treated, Eylea (aflibercept) is not used in combination with Beovu (brolucizumab-dbll), Byooviz (ranibizumab-nuna), Cimerli (ranibizumab-eqrn), Lucentis (ranibizumab), Macugen (pegaptanib), Pavblu (aflibercept- ayyh), Susvimo (ranibizumab), or Vabysmo (faricimab-svoa)</li> </ul>	
	Eylea (aflibercept) may be considered medically necessary for treatment of retinopathy of prematurity (ROP).	

Drug	Medical Necessity	
	<b>Note:</b> For bevacizumab no review is needed for eye-related injections. Reference to bevacizumab includes the biosimilars (e.g., bevacizumab- adcd, bevacizumab-awwb, bevacizumab-bvzr, and bevacizumab-maly)	
Eylea HD (aflibercept)	<ul> <li>Eylea HD (aflibercept) may be considered medically necessary for the following: <ul> <li>Neovascular (Wet) Age-Related Macular Degeneration (AMD)</li> <li>Diabetic Macular Edema (DME)</li> <li>Diabetic Retinopathy (DR)</li> </ul> </li> <li>AND <ul> <li>The individual has tried bevacizumab and had an inadequate response or intolerance to bevacizumab</li> </ul> </li> <li>AND <ul> <li>Per each eye treated, Eylea HD (aflibercept) is not used in combination with Beovu (brolucizumab-dbll), Byooviz (ranibizumab-nuna), Cimerli (ranibizumab-eqrn), Lucentis (ranibizumab), Macugen (pegaptanib), Pavblu (aflibercept-ayyh), Susvimo (ranibizumab), or Vabysmo (faricimab-svoa)</li> </ul> </li> </ul>	
	Note: For bevacizumab no review is needed for eye-related injections. Reference to bevacizumab includes the biosimilars (e.g., bevacizumab- adcd, bevacizumab-awwb, bevacizumab-bvzr, and bevacizumab-maly)	
Lucentis (ranibizumab)	Lucentis (ranibizumab) may be considered medically necessary	
	for the following:	
	Neovascular (Wet) Age-Related Macular Degeneration (AMD)	
	Macular Edema Following Retinal Vein Occlusion (RVO)	
	Diabetic Macular Edema (DME)	
	Diabetic Retinopathy (DR)	
	Myopic Choroidal Neovascularization (mCNV)	
	AND	
	The individual has they bevacizumab and had an inadequate response or intolerance to bevacizumab	
	Per each eve treated. Lucentis (ranibizumab) is not used in	
	combination with Beovu (brolucizumab-dbll). Evlea/Evlea HD	
	(aflibercept), Macugen (pegaptanib), Pavblu (aflibercept-avvh).	
	Susvimo (ranibizumab), or Vabysmo (faricimab-svoa)	



Drug	Medical Necessity	
	<b>Note:</b> For bevacizumab no review is needed for eye-related injections. Reference to bevacizumab includes the biosimilars (e.g., bevacizumab- adcd, bevacizumab-awwb, bevacizumab-bvzr, and bevacizumab-maly)	
Macugen (pegaptanib)	Macugen (pegaptanib) may be considered medically necessary	
	for the following:	
	Neovascular (Wet) Age-Related Macular Degeneration (AMD)	
	The individual has tried bevacizumab and had an inadequate	
	response or intolerance to bevacizumab	
	AND	
	• Per each eye treated, Macugen (pegaptand) is not used in combination with Beovu (brolucizumab-dbll). Byooviz	
	(ranibizumab-nuna) Cimerli (ranibizumab-egrn) Evlea/Evlea	
	HD (aflibercept), Lucentis (ranibizumab), Payblu (aflibercept-	
	avyh), Susvimo (ranibizumab), or Vabysmo (faricimab-svoa)	
	<b>Note</b> : For bevacizumab no review is needed for eye-related injections. Reference to bevacizumab includes the biosimilars (e.g., bevacizumab- adcd, bevacizumab-awwb, bevacizumab-bvzr, and bevacizumab-maly)	
Pavblu (aflibercept-ayyh)	Pavblu (aflibercept-ayyh) may be considered medically	
	necessary for the following:	
	Neovascular (Wet) Age-Related Macular Degeneration (AMD)	
	Diabetic Macular Edema (DME)	
	Diabetic Retinopathy (DR)	
	Macular Edema Following Retinal Vein Occlusion (RVO)	
	AND	
	<ul> <li>The individual has tried bevacizumab and had an inadequate</li> <li>response or intolerance to howacizumab</li> </ul>	
	<ul> <li>Per each eve treated, Pavblu (aflibercept-avvh) is not used in</li> </ul>	
	combination with Beovu (brolucizumab-dbll), Byooviz	
	(ranibizumab-nuna), Cimerli (ranibizumab-eqrn), Eylea/Eylea	
	HD (aflibercept), Lucentis (ranibizumab), Macugen	
	(pegaptanib), Susvimo (ranibizumab), or Vabysmo (faricimab- svoa)	



Drug	Medical Necessity	
	<b>Note:</b> For bevacizumab no review is needed for eye-related injections. Reference to bevacizumab includes the biosimilars (e.g., bevacizumab- adcd, bevacizumab-awwb, bevacizumab-bvzr, and bevacizumab-maly)	
Susvimo (ranibizumab)	Susvimo (ranibizumab) may be considered medically necessary	
	for the following:	
	Neovascular (Wet) Age-Related Macular Degeneration (AMD)	
	Diabetic Macular Edema (DME)	
	AND	
	The individual has tried bevacizumab and had an inadequate	
	response or intolerance to bevacizumab	
	AND	
	<ul> <li>Has previously responded to at least two intravitreal injections of a VEGF inhibitor</li> </ul>	
	AND	
	• Per each eye treated, Susvimo (ranibizumab) is not used in	
	combination with Beovu (brolucizumab-dbll), Byooviz	
	(ranibizumab-nuna), Cimerli (ranibizumab-eqrn), Eylea/Eylea	
	HD (aflibercept), Lucentis, (ranibizumab), Macugen	
	(pegaptanib), Pavblu (aflibercept-ayyh), or Vabysmo (faricimab- svoa)	
	<b>Note:</b> For bevacizumab no review is needed for eye-related injections. Reference to bevacizumab includes the biosimilars (e.g., bevacizumab- adcd, bevacizumab-awwb, bevacizumab-bvzr, and bevacizumab-maly)	
Vabysmo (faricimab-svoa)	Vabysmo (faricimab-svoa) may be considered medically	
	necessary for the following:	
	Neovascular (Wet) Age-Related Macular Degeneration (AMD)	
	Diabetic Macular Edema (DME)	
	Macular Edema Following Retinal Vein Occlusion (RVO)	
	AND	
	The individual has tried bevacizumab and had an inadequate	
	response or intolerance to bevacizumab	
	AND Der each eve treated Veburne (farigingh greet) is not used in	
	<ul> <li>Fer each eye treated, vabysmo (lancimab-svoa) is not used in combination with Beovu (brolucizumab-dbll). Byooviz</li> </ul>	
	<ul> <li>Per each eye treated, Vabysmo (faricimab-svoa) is not used in combination with Beovu (brolucizumab-dbll), Byooviz</li> </ul>	



Drug	Medical Necessity
	(ranibizumab-nuna), Cimerli (ranibizumab-eqrn), Eylea/Eylea HD (aflibercept), Lucentis (ranibizumab), Macugen (pegaptanib), Pavblu (aflibercept-ayyh), or Susvimo (ranibizumab)
	<b>Note:</b> For bevacizumab no review is needed for eye-related injections. Reference to bevacizumab includes the biosimilars (e.g., bevacizumab- adcd, bevacizumab-awwb, bevacizumab-bvzr, and bevacizumab-maly)

Drug	Investigational
As listed	The medications listed in this policy are subject to the product's US Food and Drug Administration (FDA) dosage and administration prescribing information.
	All other uses of the drugs listed for conditions not outlined in this policy are considered investigational.

Length of Approval		
Approval	Criteria	
Initial authorization	Non-formulary exception reviews and all other reviews for all drugs listed in policy may be approved up to 12 months.	
Re-authorization criteria	Non-formulary exception reviews and all other reviews for all drugs listed in policy may be approved up to 12 months as long as the drug-specific coverage criteria are met and chart notes demonstrate that the individual continues to show a positive clinical response to therapy.	

### **Documentation Requirements**

The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following:

• Office visit notes that contain the diagnosis, relevant history, medication history, and physical evaluation

AND



#### **Documentation Requirements**

• Documentation that the individual has tried bevacizumab and had an inadequate response or intolerance to bevacizumab

# Coding

Code	Description
HCPCS	
J0177	Injection, aflibercept hd (Eylea HD) 1 mg
J0178	Injection, aflibercept (Eylea), 1 mg
J0179	Injection, brolucizumab-dbll (Beovu,) 1 mg
J2503	Injection, pegaptanib sodium (Macugen), 0.3 mg
J2777	Injection, faricimab-svoa (Vabysmo), 0.1 mg
J2778	Injection, ranibizumab (Lucentis), 0.1 mg
J2779	Injection, ranibizumab, via intravitreal implant (Susvimo) 0.1 mg
J3590	Unclassified biologics
Q5124	Injection, ranibizumab-nuna, biosimilar (Byooviz) 0.1 mg
Q5128	Injection, ranibizumab-eqrn biosimilar (Cimerli) 0.1 mg
Q5147	Injection, aflibercept-ayyh (Pavblu), biosimilar, 1 mg (new code effective 04/01/25)

**Note:** CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

### **Related Information**

# **Benefit Application**

All medications listed in this policy are managed through the medical benefit.



### Background

Age-related macular degeneration is a disorder of the macula that is characterized by the presence of at least intermediate-size drusen (>63µm in diameter), retinal pigment epithelium (RPE) abnormalities (i.e. hypopigmentation or hyperpigmentation), and/or the presence of geographic atrophy of the RPE, choroidal neovascularization ([CNV] exudative, wet), polypoidal choroidal vasculopathy (PCV), reticular pseudodrusen, or retinal angiomatous proliferation. Choroidal neovascularization or wet AMD (nAMD), is characterized by growth of abnormal vessels into the subretinal space, typically from the choroidal circulation, but sometimes from the retinal circulation. It is estimated that 0.46% of the global population has nAMD based on results from a pooled meta-analysis. However, nAMD accounts for more than 80% of AMD cases that result in severe visual loss or legal blindness. The greatest risk factor for AMD is aging, but other risk factors include Caucasian race, smoking, alcohol use, diets deficient in fruits, vegetables, and fish, family history, cardiovascular disease, AIDS, chronic myeloproliferative diseases, and cataract surgery. Thus, the prevalence of AMD in the United States is expected to increase to 22 million individuals by 2050.

### **Summary of Evidence**

# Meaningful Differences in Efficacy in Clinical Trials

Treatment with a VEGF inhibitor has demonstrated favorable visual acuity outcomes compared to no treatment for nAMD. Efficacy outcomes are relatively similar, in terms of visual acuity, measured by stable vision (<15 letter loss) and mean gain in best corrected visual acuity (BCVA) in early treatment diabetic retinopathy study (ETDRS) letters from baseline with aflibercept, bevacizumab, brolucizumab, and ranibizumab. Pegaptanib did not demonstrate improvements in visual acuity, as evidenced by only 55% of individuals experiencing vision loss of <15 letters. On the other hand, aflibercept has demonstrated statistically significant improvements in anatomical outcomes, as assessed by mean reductions in CRT.

## Meaningful Differences in Safety Profiles

Serious adverse event rates were relatively similar between aflibercept, bevacizumab, faricimab, and ranibizumab in clinical trials. While adverse event rates between brolucizumab and aflibercept were similar in clinical trials, the ASRS released a statement in February 2020 regarding the safety of brolucizumab due to 14 cases of vasculitis (11 of which were designated occlusive retinal vasculitis) being reported since its FDA approval in October 2019. Higher rates of serious adverse events were observed in the pegaptanib clinical trials than the other VEGF inhibitor therapies.

### **Real World Comparative Effectiveness**

A Cochrane, systematic review, was published comparing the efficacy and safety of VEGF inhibitors (pegaptanib, ranibizumab, and bevacizumab) to the control of no treatment for the indication of neovascular age-related macular degeneration.

# Vascular Endothelial Growth Factor Inhibitor Treatment Versus Control for Neovascular Age-Related Macular Degeneration

- Mean change in visual acuity was measured by average mean gain in early treatment diabetic retinopathy study (ETDRS) letters of 6.72, 17.80, 12.60 letters with pegaptanib, ranibizumab, and bevacizumab, respectively. In comparison, the control group was observed to have mean losses between 10-16 ETDRS letters.
- Mean differences of combined (pegaptanib, ranibizumab, and bevacizumab) National Eye Institute-Visual Function Questionnaire (NEI-VFQ) scores compared to the control were 6.69 points higher.
- A risk ratio range of 0.17 to 2.08 for the occurrence of serious systemic adverse events was calculated for individuals receiving VEGF inhibitor therapy, relative to the control.
- A risk ratio range of 0.52 to 2.71 for the occurrence of serious ocular adverse events at 1 year was calculated for individuals receiving VEGF inhibitor therapy, relative to the control.
- Thus, VEGF inhibitor treatment appears to significantly improve visual acuity and may reduce adverse events compared to the control of no treatment for nAMD with moderate to high grades of evidence.

### Bevacizumab Versus Ranibizumab for Neovascular Age Related Macular Degeneration

- The risk ratio for a gain of >15 letters visual acuity at 1 year was 0.95 for bevacizumab compared to ranibizumab.
- The risk ratio for a loss of <15 letters visual acuity at 1 year was 1.00 for bevacizumab compared to ranibizumab.
- Mean difference in visual acuity, as measured by number of ETDRS letters at 1 year, was calculated to be -0.6 letters with bevacizumab compared to ranibizumab.
- Mean difference in reduction of central retinal thickness (CRT) at year 1 was calculated to be -11.6µm with bevacizumab compared to ranibizumab
- A risk ratio range of 0.96 to 1.02 was calculated for having no problems in quality of life domains at 1 year with bevacizumab compared to ranibizumab.
- The risk ratio for serious systemic adverse events at 1 year was calculated to be 1.15 with bevacizumab compared to ranibizumab.
- A risk ratio range of 0.51 to 7.05 for serious ocular adverse events at 1 year was calculated when comparing bevacizumab and ranibizumab. Individually, their risks were observed to be <5 events per 1000 individuals.
- The efficacy and safety outcomes between bevacizumab and ranibizumab appear to be comparable with moderate to high quality grades of evidence.

### **Combination VEGF and Ang-2 Inhibitors**

Faricimab neutralizes angiopoietin-2 (Ang-2) and vascular endothelial growth factor A (VEGF-A) via both simultaneous and independent binding. This is the first in class drug that targets two distinct pathway. The primary evidence for efficacy for neovascular (wet) age-related macular degeneration (nAMD) of faricimab stems from two randomized, active comparator phase III clinical trials: TENAYA and LUCERNE, and two randomized active comparator phase II clinical trial STAIRWAY and AVENUE. The STAIRWAY trial demonstrated the efficacy and safety of faricimab in the treatment of adults with nAMD. One-year results of the primary outcomes of TENAYA and LUCERNE was announced during the press conference. The results showed noninferiority

comparing to aflibercept even at longer intervals. From STAIRWAY trial, faricimab dosing every 16 weeks and every 12 weeks resulted in maintenance of initial vision and anatomic improvements comparable with monthly ranibizumab at week 56. AVENUE trial did not show superiority of faricimab over ranibizumab in BCVA at week 36 but still support pursuing phase III trials for a potential alternative to monthly anti-VEGF therapy. Faricimab showed no new or unexpected safety signals.

The primary evidence for efficacy for diabetic macular edema of faricimab was from two randomized, active comparator phase III clinical trials: YOSEMITE and RHINE, and randomized active comparator phase II clinical trial: BOULEVARD. Both studies met their primary endpoint with faricimab consistently shown to offer non-inferior visual acuity gains to aflibercept. In YOSEMITE, the average vision gains from baseline were +11.6 and +10.7 eye chart letters in the faricimab personalized treatment interval (PTI) and two-month arms, respectively, and +10.9 letters in the aflibercept arm. In RHINE, the average vision gains from baseline were +10.8 and +11.8 letters in the faricimab PTI and two-month arms, respectively, and +10.3 letters in the aflibercept arm. The BOULEVARD trial met its primary end point; faricimab demonstrated statistically superior visual acuity gains versus ranibizumab at week 24 in treatment-naïve individuals. Central subfield thickness reduction, diabetic retinopathy severity scale (DRSS) score improvement, and extended durability outcomes support the primary outcome. These findings suggest the benefit of simultaneous inhibition of Ang-2 and VEGF-A with faricimab for individuals with DME.

# Quality of Evidence Supporting Interchangeability of These Agents

The American Academy of Ophthalmology (AAO) Preferred Practice Pattern Guidelines for AMD, updated in October 2019, considers aflibercept, bevacizumab, and ranibizumab as first-line VEGF inhibitors for the treatment of nAMD and that the selection of agent should be individually tailored based on discussions between the individual and physician.

In a combined meta-analysis and systematic review, the authors reviewed the anatomical and functional outcomes of switching from bevacizumab and ranibizumab to aflibercept for the treatment of nAMD. The authors included 28 studies and results showed small improvements in best corrected visual acuity (BCVA) of 1.11 letters (95% CI -0.25 to 2.46, P=0.17) at 6 months and 0.63 letters (95% CI -0.26 to 1.52, P=0.17) at 12 months. However, significant improvements were found in mean CRT after switching, with reductions of -61.90 $\mu$ m (95% CI -77.10 to -46.80, P<0.001) at 6 months and -50.00 $\mu$ m (95% CI -63.20 to -36.80, P<0.001) at 12 months. Thus, switching to aflibercept in the setting of treatment-resistant nAMD with bevacizumab and/or ranibizumab can be a reasonable option to consider.

### **Practice Guidelines and Position Statements**

The AAO updated their Age-Related Macular Degeneration Preferred Practice Pattern in October 2019. For the treatment of nAMD, VEGF inhibitors are considered to be first-line therapy due to improvements in visual outcomes observed in clinical trials. The AAO does not offer a recommendation on the choice of agent, stating that the choice should be individually tailored based on individual and physician discussions. Pegaptanib does not improve visual activity and is rarely used in current clinical practice. Other treatment options include photodynamic therapy, thermal laser photocoagulation, surgery, and radiation therapy.

### 2021 Update

Reviewed prescribing information for all drugs listed in policy and researched product availability. Identified a biosimilar ranibizumab product (biosimilar to Lucentis) called Byooviz (ranibizumab-nuna) and a new ranibizumab product called Susvimo (ranibizumab) which is an ocular implant that is FDA-approved for the treatment of individuals with neovascular (wet) AMD who have previously responded to at least two intravitreal injections of a VEGF inhibitor. Added Byooviz (ranibizumab-nuna) to the policy for the treatment of AMD, RVO and mCNV and added Susvimo to the policy for the treatment of AMD.

### 2022 Update

Reviewed prescribing information for all drugs listed in policy. Added coverage criteria for Vabysmo (faricimab-svoa) for the treatment of AMD and DME. Vabysmo is the first bispecific antibody designed for the eye and it targets two distinct pathways, via angiopoietin-2 (Ang-2) and vascular endothelial growth factor-A (VEGF-A), that drive many retinal conditions. Updated criteria for Beovu, Byooviz, Eylea, Lucentis, Macugen, and Susvimo to include use is not in combination with Vabysmo and to clarify combination use is per each eye treated.

### 2023 Update

Reviewed prescribing information for all drugs listed in policy. Added coverage criteria for Eylea (aflibercept) for the treatment of retinopathy of prematurity.



### 2024 Update

Reviewed prescribing information for all drugs listed in policy. Added coverage criteria for Vabysmo (faricimab-svoa) for the treatment of macular edema following retinal vein occlusion.

### 2025 Update

Reviewed prescribing information for all drugs listed in policy. Added coverage criteria for Pavblu (aflibercept-ayyh). Updated criteria for Beovu, Byooviz, Cimerli, Eylea, Eylea HD, Lucentis, Macugen, Susvimo, and Vabysmo to include use is not in combination with Pavblu. Updated Susvimo (ranibizumab) coverage criteria to require that the individual has previously responded to at least two intravitreal injections of a VEGF inhibitor. Updated Susvimo (ranibizumab) to include coverage criteria for the treatment of certain individuals with diabetic macular edema. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information.

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- 31. Beovu (brolucizumab-dbll) injection, for intravitreal use [Prescribing Information]. Novartis Pharmaceuticals Corporation; East Hanover, New Jersey. Revised September 2023.
- 32. Byooviz (ranibizumab-nuna) injection, for intravitreal use [Prescribing Information]. Biogen Inc.; Cambridge, MA. Revised July 2024.
- 33. Cimerli (ranibizumab-eqrn) injection, for intravitreal use [Prescribing Information]. Coherus BioSciences, Inc.; Redwood City, CA. Revised June 2024.
- 34. Eylea (aflibercept) injection, for intravitreal use [Prescribing Information]. Regeneron Pharmaceuticals, Inc.; Tarrytown, NY. Revised October 2024.
- 35. Eylea HD (aflibercept) injection, for intravitreal use [Prescribing Information]. Regeneron Pharmaceuticals, Inc.; Tarrytown, NY. Revised October 2024.
- 36. Lucentis (ranibizumab injection) for intravitreal injection [Prescribing Information]. Genentech Inc.; South San Francisco, CA. Revised February 2024.
- 37. Macugen (pegaptanib sodium injection) intravitreal injection [Prescribing Information]. Gilead Sciences, Inc.; San Dimas, CA. Revised July 2016.
- 38. Susvimo (ranibizumab injection) for intravitreal use via Susvimo ocular implant [Prescribing Information]. Genentech Inc.; South San Francisco, CA. Revised February 2025.
- 39. Vabysmo (faricimab-svoa) intravitreal injection [Prescribing Information]. Genentech Inc.; South San Francisco, CA. Revised July 2024.
- 40. Pavblu (aflibecept-ayyh) intravitreal injection [Prescribing Information]. Amgen Inc.; Thousand Oaks, CA. Revised August 2024.

### History

Date	Comments
12/01/20	New policy, approved November 10, 2020, effective for dates of service on or after March 3, 2021, following 90-day provider notification. Includes Beovu (brolucizumab- dbll) for AMD; Eylea (aflibercept) for AMD, RVO, DME, and DR; Lucentis (ranibizumab) for AMD, RVO, DME, DR, and mCNV; and Macugen (pegaptanib) for AMD. HCPCS codes J0178, J0179, J2503 and J2778 are listed.
01/01/22	Annual Review, approved December 2, 2021. Added the biosimilar Byooviz (ranibizumab-nuna) to policy for the treatment of AMD, RVO and mCNV. Added



Date	Comments
	Susvimo (ranibizumab) to policy for the treatment of AMD. Updated criteria for Beovu,
	Eylea, and Macugen to include use is not in combination with Byooviz or Susvimo.
	optited criteria for Eucentis to include use is not in combination with susvinio.
04/01/22	Coding update. Added HCPC codes C9093 and Q5124.
05/01/22	Annual Review, approved April 25, 2022. Added coverage criteria for Vabysmo
	(faricimab-svoa) for the treatment of AMD and DME. Updated criteria for Beovu,
	with Vabysmo and to clarify combination use is per each eve treated. Added Vabysmo
	to HCPC J3590.
07/01/22	Coding update. Added HCPCS codes C9097 and J2779.
08/01/22	Interim Review, approved July 25, 2022. Added coverage to Beovu (brolucizumab-dbll)
	for the treatment of diabetic macular edema (DME).
10/01/22	Coding update. Added HCPCS code J2777 and removed HCPCS code J3590.
12/01/22	Interim Review, approved November 8, 2022. Added coverage criteria for the
	interchangeable biosimilar Cimerli (ranibizumab-eqrn) for the treatment of AMD, RVO,
	DME, DR, and mCNV. Updated criteria for Beovu, Eylea, Macugen, Susvimo, and Vabysmo to include use is not in combination with Cimerli. Updated the note and
	added the biosimilars bevacizumab-adcd and bevacizumab-maly. Changed the
	wording from "patient" to "individual" throughout the policy for standardization.
	Added HCPC code J3590 to report Cimerli.
04/01/23	Coding update. Added new HCPCS code Q5128 and removed HCPCS code J3590.
06/01/23	Annual Review, approved May 9, 2023. Added coverage criteria for Eylea (aflibercept)
	for the treatment of retinopathy of prematurity.
11/01/23	Interim Review, approved October 10, 2023. Added coverage criteria for Eylea HD
	(aflibercept), a higher dose and longer acting formulation of Eylea, for the treatment of
	Susvimo, and Vabvsmo to include use is not in combination with Evlea HD. Removed
	termed HCPCS codes C9093 and C9097, and added HCPCS code J3590 for Eylea HD.
01/01/24	Coding update. Added new HCPCS code C9161.
04/01/24	Annual Review, approved March 12, 2024. Added coverage criteria for Vabysmo
	(faricimab-svoa) for the treatment of macular edema following retinal vein occlusion.
	Added new HCPCS code J0177 and termed C9161.
04/01/25	Annual Review, approved March 11, 2025. Added coverage criteria for Pavblu
	(atlibercept-ayyh). Updated criteria for Beovu, Byooviz, Cimerli, Eylea, Eylea HD,
	Pavblu. Updated Susvimo (ranibizumab) coverage criteria to require that the individual
	has previously responded to at least two intravitreal injections of a VEGF inhibitor.
	Updated Susvimo (ranibizumab) to include coverage criteria for the treatment of
	certain individuals with diabetic macular edema. Clarified that non-formulary

Date	Comments
	exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information. Added new HCPCS code Q5147.

**Disclaimer**: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2025 Premera All Rights Reserved.

**Scope**: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.

